

Stavrianopoulos et al.  
Serial No.: 08/486,070  
Filed: June 7, 1995  
Page 39 [(Fifth Supplemental Amendment (Following Applicants' August 20, 1999  
Fourth Supplemental Amendment and Their November 1, 1999 Communication)  
- December 10, 1999]

REMARKS

Claims 183-318 and 325-400 were previously pending in this application. Claims 183, 231 and 271 have been amended. Claims 401-717 have been added. Accordingly, claims 183-318 and 325-717 are being presented for further examination on the merits.

Applicants' undersigned attorney sincerely appreciates the courtesy and time extended by Examiner Ardin H. Marschel, Ph.D. in the personal interview held on December 14, 1999 to discuss this application. Dr. Dean L. Engelhardt, Senior Vice President of Enzo Biochem, Inc. also attended the interview. The changes and additions to the claims above implement some suggestions which were discussed at the December 14th interview, as well as at the previous interview held on August 3, 1999.

In a sincere effort to expedite the prosecution of this application either by obviating or narrowing any remaining issue, and thereby place the present claims in allowable conditions, Applicants have amended claims 183, 231 and 271 above. New claims 401-717 have been added, each new claim of which ultimately recites or defines additional claim elements believed to distinguish Applicants' invention over the prior art of record. As discussed *infra*, with the exception of language presented in the various independent claims, new claims 401-717 mimic and correspond to the previously pending claims, leaving out, of course, claims directed to arrays or collection or sets of arrays.

In the December 8, 1999 Examiner Interview Summary Record, it was indicated that "[w]e discussed Kourilsky et al. [GB 2,019,408] regarding overcoming the art rejection as possibly by amending clm 183, e.g., into either multiple claims and/or negating centrifugal immobilization. Arguments and/or amendments are expected soon."

Thus, claims 183, 231 and 271 - each being independent - have been amended to clarify the compositions and system defined therein. As

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amended above, each of these three claims recite "wherein quantitation is or may be performed when said double-stranded oligonucleotide or polynucleotide is still fixed or immobilized to said solid support" [in the case of claims 183 and 271] or "said system" [in the case of claim 231]. The foregoing language was suggested by the Examiner during the previous August 3, 1999 interview. With implementation of the amendments to claims 183, 231 and 271, all of the previously pending claims, 183-318 and 325-400, are similarly defined with respect to the quantitation being performed when the double-stranded oligonucleotide or polynucleotide is still fixed or immobilized.

New claims 401-717 have also been added to further clarify Applicants' claimed invention. The new claims may be conveniently divided into two sets of claims if for no other reason than to streamline the instant analysis. The first set of claims, 401-560, are directed to the negative "non-centrifugal" distinction referenced in the December 8, 1999 Summary Record. Claims 401, 449 and 489 are the independent claims in the first set. Each of these three independent claims recites language "wherein when fixation or immobilization is direct, said double-stranded oligonucleotide or polynucleotide is non-centrifugally fixed or immobilized to said solid support" [in the case of claims 401 and 489] or "said system" [in the case of claim 449]. As briefly discussed during the December 8, 1999 interview, centrifugation is disclosed in Applicants' specification in a discussion of extraction or purification methods for concentrating nucleic acids. The discussion is found in the "Summary of the Invention, beginning on page 9, last paragraph, and continuing through page 10, first paragraph. There, Applicants disclose:

Analytes to be detected by the detection processes of this invention may be present in any biological or non-biological sample, such as clinical samples, for example, blood urine, feces, saliva, pus, semen, serum, other tissue samples, fermentation broths, culture media, and the like. If necessary, the analyte may be pre-extracted or purified by known methods to concentrate its nucleic acids. Such nucleic acid concentration procedures include, for example, phenol extraction, treatment with chloroform-isoamyl alcohol or chloroform-octanol, column chromatography (e.g., Sephadex, hydroxyl apatite), and CsCl equilibrium centrifugation. *The analyte, separated from contaminating materials, if present is, according to the present invention, fixed in hybridizable form to a solid support.*

[emphasis added]

It is believed that the foregoing disclosure provides a proper basis for introducing the negative limitation into the claims with regard to the oligonucleotide or polynucleotide being "non-centrifugally fixed or immobilized" when fixation or immobilization to the solid support [or system] is direct.

Finally, the second set of new claims, 561-717, are directed to another embodiment in which the claimed compositions or system define a double-stranded oligonucleotide or polynucleotide [or double-stranded nucleic acid] in which one strand is directly or indirectly fixed or immobilized to the solid support [or system], and the other strand is fixed or immobilized through hybridization with the one strand. Thus, claim 561 which is independent defines as an element "a double-stranded oligonucleotide or polynucleotide, one strand of which is directly or indirectly fixed or immobilized to said solid support, and the other strand of which is fixed or immobilized through hybridization with said one strand." Similar language is also present in new claims 608 and 647, which are likewise independent. By defining claims 561, 608 and 647 in this way, Applicants have incorporated the language of dependent claim 201. The latter claim recites "wherein one of said oligonucleotide or polynucleotide strands is directly or indirectly fixed or immobilized to the solid support. Although the language in new claims 561-717 was not specifically discussed at either the December 8th or August 3rd interviews, it is believed that the fact that one of the nucleic acid strands in Applicants' claimed invention is directly or indirectly fixed or immobilized, and the other strand is fixed or immobilized by virtue of its hybridization with the former strand, serves as a basis for distinguishing the present invention from the prior art cited of record.

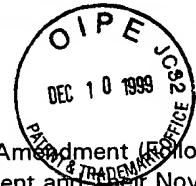
Entry of the foregoing amendments and newly added claims is respectfully requested.

Favorable action on the merits is also respectfully requested.

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### SUMMARY AND CONCLUSIONS

Claims 183-318 and 325-717 are being presented for further examination on the merits. Claims 183, 231 and 271 have been amended, and claims 401-717 have been added.

The fee for adding new claims 401-717 is \$6,390, based upon the addition of 316 new claims [316 additional claims X \$18 per claim = \$5,688], and 9 new independent claims [9 X \$78 = \$702]. The Patent and Trademark Office is hereby authorized to charge the amount of \$6,390 to Deposit Account No. 05-1135. No other fee or fees are believed due in connection with this Fifth Supplemental Amendment. In the event that any other fee or fees are due, however, either in connection with this Fifth Supplemental Amendment or with any of Applicants' previous filings, The Patent and Trademark Office is hereby authorized to charge the amount of any such fee(s) to Deposit Account No. 05-1135, or to credit any overpayment thereto.

If it would be helpful to expediting the prosecution of this application, the undersigned may be contacted by telephone at 212-583-0100 during the daytime business hours.

Favorable action on this application is respectfully sought.

Respectfully submitted

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